REMARKS

Claims 1, 4, 52, 64-69, and 85-113 are pending in the application. No amendments have been made by the present response.

Claim Objections

At page 2 of the Office Action, the Examiner requested amendments to claims 66 and 96 to recite "wherein the synthetic polymeric matrix comprises a biodegradable copolymer." Applicants have not presented the requested amendments for at least two reasons. First, the proposed amendments are improper because the phrase "the synthetic polymeric matrix" lacks antecedent basis in the claims from which claims 66 and 96 depend. Second, applicants are not aware of any defects in current claims 66 and 96 and the Office Action has not alleged there to be any specific defects.

Statement Concerning Common Ownership

In the Response to Advisory Action filed on October 29, 2009, applicants filed the following Statement Concerning Common Ownership ("the Statement"):

> Application serial number 09/909,460 and U.S. Patent No. 5,783,567 were, at the time the currently claimed invention was made, owned by, or subject to an obligation of assignment to, Pangaea Pharmaceuticals, Inc. All of the inventors of U.S. Patent No. 5,783,567 assigned their rights in the patent to Pangaea Pharmaceuticals, Inc. in an assignment recorded in the U.S. Patent & Trademark Office on August 18, 1997, at Reel 8672, Frame 0675. All of the inventors of Application serial number 09/909,460 assigned their rights in the application to Pangaea Pharmaceuticals, Inc. in an assignment recorded in the U.S. Patent & Trademark Office on September 13, 1999, at Reel 010225, Frame 0212. Application serial number 09/909,460 and U.S. Patent No. 5,783,567 were both subsequently assigned to and are currently commonly owned by Eisai Inc.

The present Office Action asserted that the Statement was defective, stating that "[i]t is applicants contention that the subject matter was invented with PCT/US98/01999 1/22/1998 and hence the statement above does not indicate that the inventions were commonly owned at the time the invention was made as the assignment of 09/909460 was made 9/13/1999."

Applicants respectfully submit that the Statement properly established common ownership so as to disqualify U.S. Patent No. 5,783,567 as prior art under 35 U.S.C. 103(c). According to MPEP 706.02(l)(2), an application and patent will be considered by the examiner to be owned by, or subject to an obligation of assignment to the same person, at the time the invention was made, if an attorney of record makes a statement that the application and the patent were, at the time the invention was made, owned by, or subject to an obligation of assignment to, the same person. Consistent with MPEP 706.02(l)(2), the Statement declared that that "[a]pplication serial number 09/909,460 and U.S. Patent No. 5,783,567 were, at the time the currently claimed invention was made, owned by, or subject to an obligation of assignment to, Pangaea Pharmaceuticals, Inc." This declaration is all that is required to establish common ownership and directly contradicts the Office Action's assertion that "the statement above does not indicate that the inventions were commonly owned at the time the invention was made." Issues such as the priority date of the claims and the details of assignment recordation do not negate the statement of common ownership.

In addition to explaining the required content of a statement of common ownership, MPEP 706.02(l)(2) also states that "Applicants may, but are not required to, submit further evidence, such as assignment records, affidavits or declarations by the common owner, or court decisions, *in addition to* the above-mentioned statement concerning common ownership" (emphasis in original). Consistent with the MPEP's instruction, the Statement merely referred to the recorded assignments for Application serial number 09/909,460 and U.S. Patent No. 5,783,567 in addition to containing the required statement of common ownership.

In view of the foregoing remarks, applicants respectfully request that the Examiner withdraw the citation of U.S. Patent No. 5,783,567 in the rejection under 35 U.S.C. 103(a).

35 U.S.C. § 102(b) (McElligott)

At page 3 of the Office Action, claims 1, 4, 85, 88, 90-93, 95-100, 102, and 103 were rejected as anticipated by McElligott, WO 94/23738.

Applicants respectfully traverse the rejection in view of the following remarks.

The present application places significant emphasis on the importance of obtaining microparticles having a high degree of supercoiled nucleic acid (see, e.g., specification at page 43, lines 30-33, stating "[t]he microparticle formation procedure was deemed successful if the incorporated DNA retained a high percentage of supercoiled DNA relative to the input DNA"). For plasmid DNA, maximizing the percentage of DNA molecules that are supercoiled results in plasmids that are more efficient at transfection as compared to non-supercoiled (i.e., nicked, linear, or otherwise damaged) plasmids.

The specification contains extensive teaching of methods that can be used to prepare microparticles having a high percentage of nucleic acid present as supercoiled circular plasmid DNA. For example, as a means of protecting the integrity of nucleic acids, the specification describes techniques that minimize the shearing forces to which nucleic acids are exposed and limit sonication times during the process of microparticle formation. This balance between sonication time and intensity permits the formulation of microparticles containing a high percentage of supercoiled plasmid DNA. The specification also contains working examples demonstrating that factors such as resuspension of plasmid DNA in Tris-EDTA buffer (page 51, lines 18-30), use of increased pH (page 52, line 27, to page 53, line 10), and/or inclusion of a stabilizer compound (page 54, line 1, to page 55, line 10) can be used during microparticle preparation so as to enhance the percentage of supercoiled DNA present in the resultant microparticles. Consistent with the inventors' discovery that nucleic acid-containing microparticles having an appropriate size for phagocytosis can be made without significantly adversely affecting nucleic acid integrity, the claimed microparticles and microparticle preparations require that at least 50% nucleic acid of the formed microparticles be present as supercoiled circular plasmid DNA.

McElligott describes methods of encapsulating nucleic acids linked to or co-existing with other molecules that facilitate uptake or integration of genetic material into cells. Nothing in McElligott indicates that the microparticles described therein were formed in such a way that at least 50% of the nucleic acid molecules are supercoiled circular plasmid DNA, as is required by the pending claims. For example, Example 1 of McElligott states that the reaction components were "vigorously agitated" and then subjected to sonication following the vigorous agitation. McElligott at page 32, lines 3-16. As explained in the enclosed publication of Ando et al. (copy enclosed as Exhibit A), standard double emulsion techniques for preparing poly(d,l-lactic-co-glycolic acid) (PLGA) microspheres cause nicking of supercoiled DNA to such an extent that the resulting microspheres have a supercoiled DNA content of approximately 39%. See Exhibit A at page 129. The Office Action has identified nothing in the microparticle preparation methods of McElligott that is alleged to overcome the problems associated with standard double emulsion techniques so as to achieve the level of supercoiling required by the currently claimed invention.

In view of the foregoing comments, applicants respectfully submit that McElligott does not anticipate claims 1, 4, 85, 88, 90-93, 95-100, 102, and 103. Applicants request that the Examiner withdraw the rejection.

35 U.S.C. § 103(a) (McElligott and Hedley et al. in view of Balland et al. and Knepp et al.)

At pages 3-6 of the Office Action, claims 1, 4, 52, 64-69, and 85-113 were rejected as unpatentable over McElligott and Hedley et al., U.S. Patent No. 5,783,567 in view of Balland et al. (1996) NATO ASI Series 290:131-42 ("Balland") and Knepp et al, U.S. Patent No. 6,264,990 ("Knepp").

Applicants respectfully traverse the rejection in view of the following remarks.

Hedley et al., U.S. Patent No. 5,783,567

As established in the section above entitled "Statement Concerning Common Ownership," Application serial number 09/909,460 and U.S. Patent No. 5,783,567 were, at the time the currently claimed invention was made, owned by, or subject to an obligation of

assignment to the same entity (Pangaea Pharmaceuticals, Inc.). The preceding section provides a detailed rebuttal to the Office Action's assertion that Statement does not indicate that the inventions were commonly owned at the time the invention was made. Because U.S. Patent No. 5,783,567 was cited as prior art under 35 U.S.C. § 102(e) in the present 35 U.S.C. § 103(a) rejection, the statement of common ownership disqualifies the reference as prior art under 35 U.S.C. § 103(c). As a result, applicants request that the Examiner withdraw the citation of Hedley et al. in the present rejection.

Knepp et al, U.S. Patent No. 6,264,990

The first paragraph of the rejection cites Knepp as a basis of rejection, but the reference is never mentioned within the substance of the rejection. As established in applicants' response to Office Action filed on May 15, 2008, Knepp does not constitute prior art against the pending claims. Knepp is presumptively entitled (according to the face of the patent) to a 35 U.S.C. §102(e) date of December 14, 1999. As acknowledged by the Examiner at page 2 of the Office Action, all of the pending claims are entitled to a priority date of January 22, 1998, the filing date of International Application Number PCT/US98/01499. Applicants request clarification as to the asserted relevance of Knepp to the present rejection.

McElligott and Balland

As detailed above in response to the anticipation rejection, McElligott does not describe a method of preparing microparticles that would have been expected to overcome the difficulties in the art and result in a microparticle composition wherein at least 50% of the nucleic acid molecules are supercoiled circular plasmid DNA, as is required by the pending claims. Balland does not cure the deficiencies of McElligott. Balland describes the adsorption of oligonucleotides (i.e., short, linear nucleic acid sequences – not circular plasmid DNA) and cetyltrimethylammonium bromide onto the surface of preformed polyisohexylcyanoacrylate particles. Balland does not disclose methods of incorporating supercoiled circular plasmid DNA into microparticles and therefore contains no teachings that would have overcome the

deficiencies of McElligott and rendered obvious the compositions of independent claims 1 or 52 or the claims that depend directly or indirectly therefrom.

In view of the foregoing comments, applicants respectfully submit that the cited references do not render obvious any of claims 1, 4, 52, 64-69, and 85-113. Applicants request that the Examiner withdraw the rejection.

CONCLUSION

Applicants submit that all grounds for rejection have been overcome and that all claims are in condition for allowance, which action is requested.

Enclosed is a Petition for Extension of Time. The extension of time fee is being paid concurrently herewith on the Electronic Filing System (EFS) by way of Deposit Account authorization. Please apply any deficiencies or credit any overpayment to deposit account 06-1050, referencing Attorney Docket No. 08190-014002.

Respectfully submitted,

Date: June 30, 2010

/Jack Brennan/
Jack Brennan
Reg. No. 47,443

Customer Number 26161
Fish & Richardson P.C.
Telephone: (212) 765-5070
Facsimile: (877) 769-7945